

Increased RBE of carbon ions in tumor growth inhibition using an in vivo lung adenocarcinoma model

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Carbon ion irradiation is an emerging therapy option for various tumor entities, including lung cancer [1]. This irradiation quality with a high linear energy transfer (LET) induces more complex and irreparable clustered DNA damage. Compared with low-LET photons and protons, carbon ions have a higher relative biological effectiveness (RBE) with less oxygen-dependent radiosensitivity [2]. Based on the colony formation assay we previously revealed a RBE of 3 for 10% cell survival in A549 cells [3].

Here we compared the effect of different irradiation qualities (carbon ions (¹²C) and photon irradiations) on the tumor growth using a mouse tumor model of the human non small lung adenocarcinoma cell line (A549).

Adult BALBc nu/nu mice were maintained under pathogen-free conditions and handled in accordance with the recommendations for animal experimentation of European Community. After subcutaneous tumor initiation and a starting tumor volume of 200 mm³, local tumor irradiation with biologically equivalent doses of ¹²C (LET 50-70 keV/μm, energy 122.36-183.74 MeV/u on target, 40 mm spread out bragg peak [SOBP]) and photons (6 MV-X) were performed. The tumor volumes were measured 3 times per week until reaching a target tumor volume of 400 mm³ or after an observation time of 40 days. The tumor volume (TV) was calculated by the formula: $TV [mm^3] = (L \times W^2)/2$; where L is the longest dimension of the tumor [mm], and W is the shortest dimension of the tumor [mm].

We found a tumor volume doubling time of 37.8 ± 1.6 days in the carbon ion irradiated group compared to 18.3 ± 1.2 days in the photon irradiated group and 11.9 ± 1.0 days in the unirradiated control group (Figure 1). Thus, the RBE of in vivo tumor growth is above 3 and clearly greater than for cell survival measurements, providing further support for a clinical application. However, it should be mentioned that 3 of 6 carbon ion irradiated tumors did not reach the target tumor volume of 400 mm³ within the observation time of 40 days.

In further experiments, we will focus on the analysis of the effects of carbon ion irradiation on the tumor micro-environment. These experiments will consider effects on tumor cells, tumor vasculature as well as distribution of immune cells.

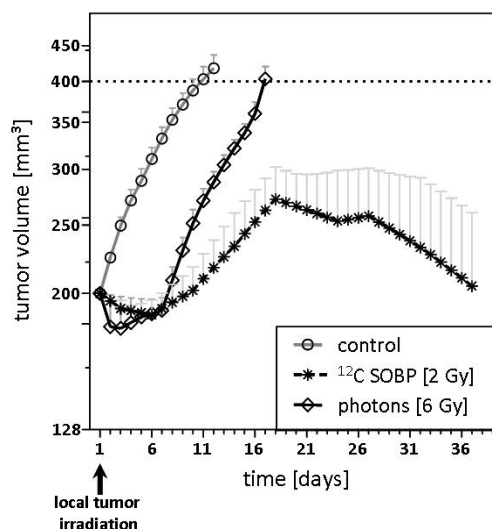


Figure 1: Growth curves of A549 tumors after irradiation with carbon ions (¹²C SOBP) or photons. All data represent the means \pm S.E.M.

References

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